

## Freeform Search

Database:

US Pre-Grant Publication Full-Text Database  
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 EPO Abstracts Database  
 JPO Abstracts Database  
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 IBM Technical Disclosure Bulletins

Term:

retention.clm. and translocat\$.clm.

Display:  Documents in Display Format:  Starting with Number Generate: ☐ Hit List ☒ Hit Count ☐ Side by Side ☐ Image

Search

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### Search History

DATE: Monday, April 12, 2004 [Printable Copy](#) [Create Case](#)

<u>Set</u> <u>Name</u>	<u>Query</u>	<u>Hit</u> <u>Count</u>	<u>Set</u> <u>Name</u> result set
side by side			
	DB=USPT; PLUR=YES; OP=AND		
<u>L1</u>	(truncat\$ or fragment\$ or delet\$ or portion\$ or domain or domains or region or regions or peptide).ti,ab,clm.	1346253	<u>L1</u>
<u>L2</u>	( a same b same (toxin or cytotoxin or adp or ribosylat\$ or exotoxin or exotoxin or pe or pea or cholera or lt or ct or ctab or ctx or heatlabile)).ti,ab,clm.	579	<u>L2</u>
<u>L3</u>	L1 same (nterminal or n-terminal or signal or secretion or 5 )	380483	<u>L3</u>
<u>L4</u>	L3 same l2	38	<u>L4</u>
<u>L5</u>	L3 same l2 same (cdna or c-dna or dna or mrna or m-rna or rna or nucleic or nuclear or nucleotide or polynucleotide or poly-nucleotide).ti,ab,clm.	9	<u>L5</u>
<u>L6</u>	(lack or deficient or delete or deletion or removal) near10 (signal or secretion or secret)	24494	<u>L6</u>
<u>L7</u>	L6 same (cdna or c-dna or dna or mrna or m-rna or rna or nucleic or nuclear or nucleotide or polynucleotide or poly-nucleotide)	1972	<u>L7</u>
<u>L8</u>	( a same b same (toxin or cytotoxin or adp or ribosylat\$ or exotoxin or exotoxin or pe or pea or cholera or lt or ct or ctab or ctx or heatlabile))	14286	<u>L8</u>
<u>L9</u>	L8 same l7	1	<u>L9</u>

<u>L10</u>	L8 and 17 not 19	408	<u>L10</u>
<u>L11</u>	L8 and 17.clm. not 19	11	<u>L11</u>
<u>L12</u>	(truncat\$ or fragment\$ or delet\$ or portion\$ or domain or domains or region or regions or peptide) same 18	4000	<u>L12</u>
<u>L13</u>	L12 same 16	16	<u>L13</u>
<u>L14</u>	L13 not 111	16	<u>L14</u>
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=AND</i>			
<u>L15</u>	ribosylat\$.ti.	46	<u>L15</u>
<u>L16</u>	adpribosylat\$.ti.	0	<u>L16</u>
<u>L17</u>	adp.ti. near3 ribosylat\$.ti.	39	<u>L17</u>
<u>L18</u>	L17 not 115	0	<u>L18</u>
<u>L19</u>	exotoxin.ti. not 117 not 115	163	<u>L19</u>
<u>L20</u>	119 and (cdna or c-dna or dna or mrna or m-rna or rna or nucleic or nuclear or nucleotide or polynucleotide or poly-nucleotide).ti.	7	<u>L20</u>
<u>L21</u>	(truncat\$ or fragment\$ or delet\$ or portion\$ or domain or domains or region or regions or peptide) same (5 or n-terminal or nterminal)	3341948	<u>L21</u>
<u>L22</u>	L21 and (115 or 117 or 119)	33	<u>L22</u>
<u>L23</u>	translocat\$.clm. same adp.clm.	12	<u>L23</u>
<u>L24</u>	l23 and (excret\$.clm. or signal.clm. or secret\$.clm. or cytoplas\$.clm.)	3	<u>L24</u>
<u>L25</u>	cholera.clm. same plant.clm.	10	<u>L25</u>
<u>L26</u>	(a2 or a-2).clm. same translocat\$.clm.	3	<u>L26</u>
<u>L27</u>	retension.clm. and translocat\$.clm. and (toxin or cytotoxin or adp or ribosylat\$ or exotoxin or exo-toxin or pe or pea or cholera or lt or ct or ctab or ctx or heatlabile).clm.	0	<u>L27</u>
<u>L28</u>	retension.clm. and translocat\$.clm.	0	<u>L28</u>
<u>L29</u>	retention.clm. and translocat\$.clm.	10	<u>L29</u>

END OF SEARCH HISTORY

## WEST Search History





DATE: Monday, April 12, 2004

Hide?	Set Name	Query	Hit Count
		<i>DB=USPT; PLUR=YES; OP=AND</i>	
<input type="checkbox"/>	L1	(truncat\$ or fragment\$ or delet\$ or portion\$ or domain or domains or region or regions or peptide) .ti,ab,clm.	1346253
<input type="checkbox"/>	L2	( a same b same (toxin or cytotoxin or adp or ribosylat\$ or exotoxin or exotoxin or pe or pea or cholera or lt or ct or ctab or ctx or heatlabile)).ti,ab,clm.	579
<input type="checkbox"/>	L3	L1 same (nterminal or n-terminal or signal or secretion or 5 )	380483
<input type="checkbox"/>	L4	L3 same l2	38
<input type="checkbox"/>	L5	L3 same l2 same (cdna or c-dna or dna or mrna or m-rna or rna or nucleic or nuclear or nucleotide or polynucleotide or poly-nucleotide).ti,ab,clm.	9
<input type="checkbox"/>	L6	(lack or deficient or delete or deletion or removal) near10 (signal or secretion or secret)	24494
<input type="checkbox"/>	L7	L6 same (cdna or c-dna or dna or mrna or m-rna or rna or nucleic or nuclear or nucleotide or polynucleotide or poly-nucleotide)	1972
<input type="checkbox"/>	L8	( a same b same (toxin or cytotoxin or adp or ribosylat\$ or exotoxin or exotoxin or pe or pea or cholera or lt or ct or ctab or ctx or heatlabile))	14286
<input type="checkbox"/>	L9	L8 same l7	1
<input type="checkbox"/>	L10	L8 and l7 not l9	408
<input type="checkbox"/>	L11	L8 and l7.clm. not l9	11
<input type="checkbox"/>	L12	(truncat\$ or fragment\$ or delet\$ or portion\$ or domain or domains or region or regions or peptide) same l8	4000
<input type="checkbox"/>	L13	L12 same l6	16
<input type="checkbox"/>	L14	L13 not l11	16
		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=AND</i>	
<input type="checkbox"/>	L15	ribosylat\$.ti.	46
<input type="checkbox"/>	L16	adpribosylat\$.ti.	0
<input type="checkbox"/>	L17	adp.ti. near3 ribosylat\$.ti.	39
<input type="checkbox"/>	L18	L17 not l15	0
<input type="checkbox"/>	L19	exotoxin.ti. not l17 not l15	163
<input type="checkbox"/>	L20	l19 and (cdna or c-dna or dna or mrna or m-rna or rna or nucleic or nuclear or nucleotide or polynucleotide or poly-nucleotide).ti.	7
<input type="checkbox"/>	L21	(truncat\$ or fragment\$ or delet\$ or portion\$ or domain or domains or region or regions or peptide) same (5 or n-terminal or nterminal)	3341948
<input type="checkbox"/>	L22	L21 and (l15 or l17 or l19)	33
<input type="checkbox"/>	L23	translocat\$.clm. same adp.clm.	12

<input type="checkbox"/>	L24	l23 and (excret\$.clm. or signal.clm. or secret\$.clm. or cytoplas\$.clm.)	3
<input type="checkbox"/>	L25	cholera.clm. same plant.clm.	10
<input type="checkbox"/>	L26	(a2 or a-2).clm. same translocat\$.clm.	3

END OF SEARCH HISTORY

## WEST Search History

DATE: Monday, April 12, 2004

Hide?	Set Name	Query	Hit Count
		<i>DB=USPT; PLUR=YES; OP=AND</i>	
<input type="checkbox"/>	L1	rdel or kdel	262
<input type="checkbox"/>	L2	L1 near25 (delet\$ or remov\$ or lack\$ or substitu\$)	32

END OF SEARCH HISTORY

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- 
- ☐ 1. [6673348](#). 27 Feb 01; 06 Jan 04. Heat shock protein-based vaccines and immunotherapies. Rothman; James E., et al. 424/184.1; 424/248.1 435/69.7 435/71.1 530/350. A61K039/00 A61K039/04.
- 
- ☐ 2. [6663868](#). 13 Feb 98; 16 Dec 03. Heat shock protein-based vaccines and immunotherapies. Rothman; James E., et al. 424/193.1; 424/195.11 424/196.11 424/197.11 424/277.1 424/278.1 514/2 514/24 530/300 530/350 530/412 530/413 530/828. A61K039/385.
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- ☐ 3. [6656679](#). 27 Feb 01; 02 Dec 03. Heat shock protein-based vaccines and immunotherapies. Rothman; James E., et al. 435/5; 424/184.1 424/248.1. C12Q001/70 A61K039/00.
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- ☐ 4. [6641812](#). 27 Feb 01; 04 Nov 03. Heat shock protein-based vaccines and immunotherapies. Rothman; James E., et al. 424/184.1; 424/248.1 435/455 435/69.7 530/350. A61K039/00 A61K039/04.
- 
- ☐ 5. [6617431](#). 17 Aug 99; 09 Sep 03. Recombinant collagen and derived proteins produced by plants, methods for obtaining them and uses. Gruber; Veronique, et al. 530/356;. C07K014/00.
- 
- ☐ 6. [6605464](#). 23 Feb 00; 12 Aug 03. Method of treatment of cancer and infectious disease and compositions useful in same. Rothman; James E., et al. 435/320.1; 435/325 435/455 435/69.1. C12N015/63.
- 
- ☐ 7. [6573431](#). 02 Jul 99; 03 Jun 03. Recombinant predudodenal lipases and polypeptides derivatives produced by plants, processes for obtaining them and their uses. Lenée; Philippe, et al. 800/295; 435/320.1 435/410 435/411 435/412 435/414 435/415 435/416 435/417 536/23.1 536/23.5 800/278 800/288 800/298 800/305 800/306 800/312 800/317 800/317.2 800/317.3 800/317.4 800/320 800/320.1 800/320.2 800/320.3 800/322. A01H005/00 C12N015/85 C07H021/04.
- 
- ☐ 8. [6392121](#). 07 Oct 99; 21 May 02. Gemini virus vectors for gene expression in plants. Mason; Hugh S., et al. 800/287; 435/252.3 435/252.33 435/320.1 435/410 435/411 435/412 435/414 435/415 435/417 435/430 435/468 435/469 435/470 536/23.1 536/23.2 536/23.6 536/24.1 800/278 800/280 800/293 800/295 800/298 800/312 800/317.2 800/317.3 800/317.4 800/320.1 800/320.2 800/320.3. C12N005/04 C12N015/82 C12N015/87 C12N015/90.
- 
- ☐ 9. [6331299](#). 13 Feb 98; 18 Dec 01. Method for treatment of cancer and infectious disease and compositions useful in same. Rothman; James E., et al. 424/93.21; 424/450 435/320.1 435/325 435/455 435/69.1. A61K048/00.
- 
- ☐ 10. [6329173](#). 21 Apr 00; 11 Dec 01. Method of intracellular binding target molecules. Marasco; Wayne A., et al. 435/69.1; 424/93.2 435/238 435/326 435/330 435/339 514/44 530/387.3 530/388.3 530/389.3. C12P021/06.
- 
- ☐ 11. [6287562](#). 08 Jan 99; 11 Sep 01. Methods of inhibiting the growth of cells bearing LewisY antigens using B1, B3, or B5 targeted immunoconjugates. Pastan; Ira, et al. 424/183.1; 424/156.1 424/178.1 424/181.1 530/387.3 530/388.8 530/388.85 530/391.1 530/391.7. A61K039/395.
- 
- ☐ 12. [6107028](#). 15 May 96; 22 Aug 00. Ribozymes for treating hepatitis C. Kay; Mark A., et al.

435/6; 435/320.1 435/366 435/370 435/91.31 536/23.1 536/24.5. C07H021/04 C12Q001/68  
C12N015/63 A61K048/00.

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□ 13. 6107027. 11 Sep 95; 22 Aug 00. Ribozymes for treating hepatitis C. Kay; Mark A., et al.  
435/6; 435/320.1 435/366 435/91.31 536/23.1 536/24.5. C07H021/04 C12Q001/68 A61K035/00  
C12N015/85.

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□ 14. 6086900. 24 Mar 98; 11 Jul 00. Methods and compositions for using membrane-penetrating  
proteins to carry materials across cell membranes. Draper; Rockford. 424/282.1; 435/320.1 435/357  
435/358 435/367 435/372.2 435/372.3 435/455 514/2 514/44 530/350 530/387.1 536/23.1 536/23.4  
536/23.5 536/23.7. A61K039/44 C12N005/10 C07K017/02.

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□ 15. 6074644. 17 Sep 99; 13 Jun 00. Nucleic acids encoding immunotoxins containing a disulfide-  
stabilized antibody fragment replacing half or more of domain IB of pseudomonas exotoxin, and  
methods of use of the encoded immunotoxins. Pastan; Ira, et al. 424/178.1; 424/236.1 530/387.3  
530/387.7 536/23.1. A61K039/395 C07K016/00.

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□ 16. 6072036. 06 Apr 99; 06 Jun 00. Method of intracellular binding of target molecules. Marasco;  
Wayne A., et al. 530/387.3; 530/387.9 530/388.35. C12P021/08.

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□ 17. 6011002. 08 Jan 97; 04 Jan 00. Circularly permuted ligands and circularly permuted chimeric  
molecules. Pastan; Ira, et al. 514/2; 436/501 514/12 530/350 530/351 530/395 530/397 530/399.  
C07K014/00 A61K038/16.

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□ 18. 6001632. 27 Oct 98; 14 Dec 99. Human protein disulfide isomerase. Braxton; Scott Michael, et  
al. 435/233; 435/252.3 435/320.1 435/69.1 530/350 536/23.2. C12N009/90 C12N001/20 C12N015/00  
C07H021/04.

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□ 19. 5990296. 03 Dec 96; 23 Nov 99. Single chain B3 antibody fusion proteins and their uses.  
Pastan; Ira, et al. 536/23.53; 435/69.1 530/387.3. C07K019/00 C07H021/04.

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□ 20. 5981726. 28 Oct 94; 09 Nov 99. Chimeric and mutationally stabilized tumor-specific B1, B3  
and B5 antibody fragments; immunotoxic fusion proteins; and uses thereof. Pastan; Ira, et al. 536/23.53;  
424/133.1 424/135.1 424/138.1 424/155.1 424/174.1 424/181.1 424/183.1 435/328 435/344 435/69.6  
435/69.7 435/91.1 530/387.3 530/387.7 530/389.7 530/391.7 536/23.4. A61K039/395 C07M021/04.

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□ 21. 5980895. 21 Aug 97; 09 Nov 99. Immunotoxin containing a disulfide-stabilized antibody  
fragment joined to a Pseudomonas exotoxin that does not require proteolytic activation. Pastan; Ira, et al.  
424/178.1; 424/236.1 530/387.3 530/387.7. A61K039/395 C07K016/00.

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□ 22. 5980886. 17 Mar 97; 09 Nov 99. Recombinant vectors for reconstitution of liver. Kay; Mark  
A., et al. 424/93.21; 424/93.1 424/93.2 514/44. A01N063/00 A01N043/04.

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□ 23. 5965371. 09 May 95; 12 Oct 99. Method of intracellular binding of target molecules. Marasco;  
Wayne A., et al. 435/7.1; 424/93.2 435/326 435/328 435/330 435/339 435/69.1 514/44. G01N033/53.

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□ 24. 5889157. 28 Oct 94; 30 Mar 99. Humanized B3 antibody fragments, fusion proteins, and uses  
thereof. Pastan; Ira, et al. 530/387.1; 424/133.1 435/328 435/7.1 530/387.3 530/387.5 530/387.7  
530/388.1 530/388.8 530/390.5 536/23.53. C07K016/00 A61K039/395.

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□ 25. 5866570. 21 Jun 94; 02 Feb 99. Treatment of vascular leakage and related syndrome such as

septic shock by administration of metalloproteinase inhibitors. Liang; Chi-Ming, et al. 514/232.2; 514/250 514/252.11. A61K031/535.

▢ 26. 5851829. 30 Mar 95; 22 Dec 98. Method of intracellular binding of target molecules. Marasco; Wayne A., et al. 435/328; 424/577 424/578 435/325 435/326 435/330 435/333 435/339 435/339.1 435/366 435/372 435/419. C12N015/00.

▢ 27. 5798249. 16 May 96; 25 Aug 98. Human protein disulfide isomerase. Braxton; Scott Michael, et al. 435/233; 435/252.3 435/320.1 435/69.1 530/350 536/23.1 536/23.2 536/23.5. C12N009/90 C07H021/02 C07H021/04 C12P021/06.

▢ 28. 5635599. 08 Apr 94; 03 Jun 97. Fusion proteins comprising circularly permuted ligands. Pastan; Ira H., et al. 530/351; 435/69.1 435/69.5 435/69.52 435/69.7 530/350. C07K019/00 C07K014/535 C07K014/55 C07K014/54.

▢ 29. 5608039. 28 Oct 94; 04 Mar 97. Single chain B3 antibody fusion proteins and their uses. Pastan; Ira, et al. 530/387.3; 435/69.1 435/69.7 435/91.1 530/387.1 530/387.5 530/387.7 530/388.1 530/388.8 530/390.5 530/866 530/867 536/23.53. C12N015/62 A61K039/00 A61K051/10 C07K016/28.

▢ 30. 5587458. 14 May 93; 24 Dec 96. Anti-erbB-2 antibodies, combinations thereof, and therapeutic and diagnostic uses thereof. King; C. Richter, et al. 530/387.3; 436/501 436/512 530/387.7 530/388.22 530/389.7 530/391.3 530/391.7. C07K016/00 C07K016/46 C07K016/28.

▢ 31. 5578466. 17 Apr 92; 26 Nov 96. Recombinant co-expression system of protein disulfide isomerase gene, yeast receptor protein ERD2 gene and a foreign product polypeptide gene, and a process for producing the foreign polypeptide using such system. Hayano; Toshiya, et al. 435/69.7; 435/254.2 435/69.1 435/69.6. C12N001/19 C12N015/14 C12N015/62.

▢ 32. 5216670. 03 Jul 91; 01 Jun 93. Message stripping protocol for a communication network. Ofek; Yoram, et al. 370/403; H04J003/24 H04L012/42.

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Terms	Documents
L1 near25 (delet\$ or remov\$ or lack\$ or substitut\$)	32

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- 
- ☐ 1. [6140082](#). 16 Aug 99; 31 Oct 00. Expression of gene products from genetically manipulated strains of bordetella. Loosmore; Sheena M., et al. 435/69.1; 435/252.3 435/320.1 435/325 435/69.8 530/350 536/23.1. C12P021/06 C07H017/00 C07K014/00.
- 
- ☐ 2. [6040427](#). 01 Jul 98; 21 Mar 00. Vaccine. Loch; Camille, et al. 530/350; 424/200.1 435/252.3 435/252.33 435/320.1 435/471 435/69.1 536/23.7. C12N015/11 C12N015/31 C12N015/70 C12N015/90 A61K039/10.
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- ☐ 3. [6022950](#). 07 Jun 95; 08 Feb 00. Hybrid molecules having translocation region and cell-binding region. Murphy; John R.. 530/350; 530/351 530/387.3 530/388.1. C07K014/00 C07K014/485 C07K014/55 C07K016/28.
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- ☐ 4. [5998168](#). 26 Jan 98; 07 Dec 99. Expression of gene products from genetically manipulated strains of bordetella. Loosmore; Sheena M., et al. 435/69.1; 435/243 435/252.3 435/325 530/350 536/23.1. C12P021/06 C07H017/00 C07K014/00.
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- ☐ 5. [5965406](#). 07 Jun 95; 12 Oct 99. Recombinant DNAs encoding three-part hybrid proteins. Murphy; John R.. 435/69.7; 435/252.33 435/320.1 536/23.4. C12N001/21 C12N015/12 C12N015/63 C12P021/02.
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- ☐ 6. [5942418](#). 01 Dec 97; 24 Aug 99. Expression of gene products from genetically manipulated strains of Bordetella. Loosmore; Sheena M., et al. 435/69.1; 435/252.3 435/320.1 536/23.1 536/24.1. C12P021/06 C07H017/00 C12N015/00.
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- ☐ 7. [5932714](#). 07 Jun 95; 03 Aug 99. Expression of gene products from genetically manipulated strains of Bordetella. Loosmore; Sheena M., et al. 536/23.7;. C07H017/00.
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- ☐ 8. [5932471](#). 30 Mar 98; 03 Aug 99. DNA encoding chimeric toxin. Williams; Diane P., et al. 435/252.3; 435/194 435/320.1 435/325 435/419 530/350 530/351 536/23.4. C12N009/12 C12N015/31 C07K014/34.
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- ☐ 9. [5863891](#). 30 Mar 98; 26 Jan 99. Chimeric toxins. Williams; Diane P., et al. 514/2; 435/194 514/12 530/350 530/351. C12N009/12 A61K038/16.
- 
- ☐ 10. [5786189](#). 11 Dec 96; 28 Jul 98. Vaccine. Loch; Camille, et al. 424/200.1; 424/254.1 435/193 435/252.3 435/252.31 435/252.33 435/252.35 435/254.2 435/320.1 435/69.1 530/403 536/23.7. C12N015/11 C12N015/31 C12N015/70 A61K039/10.
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- ☐ 11. [5763250](#). 07 Jun 95; 09 Jun 98. Chimeric toxins. Williams; Diane, et al. 435/194; 530/350 530/351. C12N009/12 C07K014/34 C07K014/52.
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- ☐ 12. [5703039](#). 07 Jun 95; 30 Dec 97. Chimeric toxins. Williams; Diane P., et al. 514/2;. A61K038/16.
- 
- ☐ 13. [5677148](#). 07 Jun 95; 14 Oct 97. DNA encoding chimeric diphtheria toxins. Williams; Diane.
-

435/69.7; 435/252.3 435/320.1 536/23.4 536/23.7. C12N015/62 C12N015/31.

☐ 14. 5668255. 04 Aug 93; 16 Sep 97. Hybrid molecules having translocation region and cell-binding region. Murphy; John R.. 530/350; 435/69.7. C07K014/00 C12P021/00.

☐ 15. 5656488. 01 Apr 94; 12 Aug 97. Recombinant avirulent salmonella antifertility vaccines. Curtiss, III; Roy, et al. 435/252.33; 424/184.1 424/200.1 435/252.3 435/252.8 435/69.3 530/395. C12N001/21 A61K045/00.

☐ 16. 5616482. 22 Apr 94; 01 Apr 97. Chimeric toxins. Williams; Diane. 435/194; 530/350 530/351. C12N009/12 C07K014/34 C07K014/52.

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- 
- ☐ 1. [20020081713](#). 04 May 01. 27 Jun 02. ADP-ribosylation factor-like proteins. Lee, Fang-Jen S., et al. 435/254.21; 435/69.1 C12N001/18 C12P021/02.
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- ☐ 2. [6562614](#). 04 May 01; 13 May 03. ADP-ribosylation factor-like proteins. Lee; Fang-Jen S., et al. 435/255.1; 435/255.2 435/471. C12N001/14 C12N015/74.
- 
- ☐ 3. [6054638](#). 03 Dec 97; 25 Apr 00. Soybean ADP ribosylation factor. McGonigle; Brian, et al. 800/298; 435/320.1 435/419 435/468 536/23.6 536/24.1 800/278 800/279 800/287 800/292 800/295. C12N015/00 C12N015/29 C12N015/82 A01H004/00.
- 
- ☐ 4. [5773688](#). 07 Apr 95; 30 Jun 98. Gene expression vector using the gene expression regulating region of the ADP ribosylation factor. Kuroda; Hisao, et al. 800/287; 435/320.1 435/421 435/468 536/24.1. C12N015/82 C12N015/63 C07H021/04 A01H005/00.
- 
- ☐ 5. [5514600](#). 27 Sep 94; 07 May 96. Mammalian guanine nucleotide binding protein with an ADP-ribosylation factor domain. Moss; Joel, et al. 436/518; 435/7.1 435/7.21 435/7.23 435/7.92 530/350 530/815 530/828. G01N033/543 C08L089/00 C12P021/02 C12N015/12.
- 
- ☐ 6. [4882146](#). 28 Mar 88; 21 Nov 89. Preventing ADP-ribosylation of G-proteins in a living subject. Shiells; Richard A., et al. 514/355; 514/263.4 514/562 514/823 514/922. A61K031/52 A61K031/44 A61K031/195.
- 
- ☐ 7. [JP02001178465A](#). 21 Dec 99. 03 Jul 01. ADP RIBOSYLATION FACTOR-LIKE PROTEIN. RI, HOJIN, et al. C12N015/09; C07K016/14 C07K016/40 C12N001/19 C12N015/02 C12P021/08.
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33. EP 369316A. immuno:toxin contg. natural human IL-2 sequence as N-terminal componen - and pseudomonas exotoxin region, and encoding dna sequence vectors and transformed cells, for treating auto:immune disease. JU, G W. A61K037/02 A61K039/00 C07H021/04 C07K013/00 C07K015/02 C12N001/20 C12N015/62 C12P021/00.

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☐ 1. Document ID: US 6673348 B2

L2: Entry 1 of 32

File: USPT

Jan 6, 2004

DOCUMENT-IDENTIFIER: US 6673348 B2

TITLE: Heat shock protein-based vaccines and immunotherapies

Detailed Description Text (4):

The term "heat shock protein," as used herein, refers to any protein which exhibits increased expression in a cell when the cell is subjected to a stress. In preferred nonlimiting embodiments, the heat shock protein is originally derived from a eukaryotic cell; in more preferred embodiments, the heat shock protein is originally derived from a mammalian cell. For example, but not by way of limitation, heat shock proteins which may be used according to the invention include BiP (also referred to as grp78), hsp/hsc70, gp96 (grp94), hsp60, hsp40, and hsp90. Especially preferred heat shock proteins are BiP, gp96, and hsp70, as exemplified below. Naturally occurring or recombinantly derived mutants of heat shock proteins may also be used according to the invention. For example, but not by way of limitation, the present invention provides for the use of heat shock proteins mutated so as to facilitate their secretion from the cell (for example having mutation or deletion of an element which facilitates endoplasmic reticulum recapture, such as KDEL or its homologs; such mutants are described in concurrently filed PCT Application No. PCT/US96/13233 (WO 97/06685), which is incorporated herein by reference).

Detailed Description Text (72):

The DNA sequence encoding a wild-type or KDEL-deleted gp96 polypeptide was subcloned from pRc/CMV into the vector pET11a (Novagen). Thus upon expression, mature gp96 could be purified from cell lysates.

Detailed Description Text (74):

PCR amplification of the sequence encoding gp96 (from pRc/CMV) was performed with the following primers. The 5' primer for both wild-type and KDEL-deleted gp96 was complementary to the DNA sequence encoding the amino terminal end of the mature form of gp96 and an Nde I restriction site (CATATG) the ATG of which forms the initiator codon:

Detailed Description Text (75):

The 3' primers were complementary to the DNA sequence of gp96 encoding the carboxyl terminal end of the protein, with the nucleotides encoding the KDEL sequence removed in the primer for the KDEL-deleted variant. Both primers contain a BamH I restriction site (GGATCC) followed by a STOP codon as shown:

Detailed Description Text (78):

This procedure is identical for wild-type or KDEL-deleted gp96. Two liters of E.

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L23: Entry 3 of 12

File: PGPB

Oct 3, 2002

DOCUMENT-IDENTIFIER: US 20020142000 A1

TITLE: Anti-CD3 immunotoxins and therapeutic uses therefor

## CLAIMS:

1. A recombinant immunotoxin polypeptide and pharmaceutically acceptable salts thereof comprising a CD3-binding domain and a Pseudomonas exotoxin (PE) mutant, said said PE mutant having ADP-ribosylating and translocation functions but substantially diminished cell-binding ability.

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L23: Entry 4 of 12

File: USPT

Nov 12, 2002

DOCUMENT-IDENTIFIER: US 6479735 B1

TITLE: Transgenic plants including a transgene consisting of a hybrid nucleic acid sequence, comprising at least one unedited mitochondrial gene fragment from higher plants and process for producing them

## CLAIMS:

1. Transgenic plants having in their nuclei an expressible hybrid sequence comprising at least one coding region of an unedited mitochondrial gene from higher plants and a sequence capable of transferring the protein expressed by the said coding region to the mitochondrion, wherein: the coding regions of the unedited mitochondrial genes are selected from the group consisting of the genes encoding a protein of the ATP synthase complex which are selected from the group consisting of the wheat ATP9 gene fragment of SEQ ID No:7 in unedited form and ligated to a mitochondrial transporter sequence, wherein the hybrid nucleic acid sequence comprising the ATP 9 gene, when transformed into a recipient plant, causes male sterility, and the wheat ATP6 gene in unedited form and ligated to a mitochondrial transporter sequence, wherein the hybrid nucleic acid sequence comprising the ATP 6 gene, when transformed into a recipient plant, causes male sterility, and the sequence capable of transferring the said expressed protein to the mitochondrion is selected from the group consisting of the fragments encoding yeast tryptophanyl tRNA synthetase, the .beta. subunit of Nicotiana plumbaginifolia ATPase, the maize ATP/ADP translocator and a 303 base pair EcoRI/KpnI fragment comprising codons 1 to 62 of subunit IV of yeast cytochrome oxidase, which hybrid sequence is capable of modifying male fertility in plants having incorporated the said transgene while not modifying the other phenotypic characteristics of the said plants.
6. Hybrid nucleic acid sequence, comprising at least the coding region of an unedited mitochondrial gene from higher plants, with which is associated a sequence capable of transferring the protein expressed by the said coding region to the mitochondrion, wherein: the coding regions of the unedited mitochondrial genes are selected from the group consisting of the genes encoding a protein of the ATP synthase complex which are selected from the group consisting of the wheat ATP9 gene fragment of Seq ID No:7 in unedited form and ligated to a mitochondrial transporter sequence, wherein the hybrid nucleic acid sequence comprising the ATP 9 gene, when transformed into a recipient plant, causes male sterility, and the wheat ATP6 gene in unedited form and ligated to a mitochondrial transporter sequence, wherein the hybrid nucleic acid sequence comprising the ATP 6A gene, when transformed into a recipient plant, causes male sterility, and the nucleic sequence capable of transferring the said expressed protein to the mitochondrion is selected from the group consisting of the fragments encoding yeast tryptophanyl tRNA synthetase, the .beta. subunit of Nicotiana plumbaginifolia ATPase, the maize ATP/ADP translocator and a 303 base pair EcoRI/KpnI fragment comprising codons 1 to 62 of subunit IV of yeast cytochrome oxidase, which hybrid sequence is capable of modifying male fertility in plants having incorporated it.
14. Process for producing male sterile transgenic plants comprising transforming a selected higher plant into a male sterile transgenic plant by introducing into a recipient plant at least one copy of the hybrid nucleic acid sequence that is

capable of modifying male fertility in plants having it incorporated therein, wherein said hybrid nucleic acid sequence comprises at least a coding region of an unedited mitochondrial gene from a higher plant, with which is associated a sequence sequence capable of transferring the protein expressed by the said coding region to the mitochondrion, wherein: the coding region of the unedited mitochondrial gene is the wheat ATP6 gene in unedited form and ligated to a mitochondrial transporter sequence, wherein the hybrid nucleic acid sequence comprising the ATP 6 gene, when transformed into a recipient plant, causes male sterility; and wherein the nucleic acid sequence capable of transferring the said expressed protein to the mitochondrion is selected from the group consisting of: the fragments encoding yeast yeast tryptophanyl tRNA synthetase, the beta sub-unit of *Nicotiana plumbaginifolia* ATPase, the maize ATP/ADP translocator, and a 303 base pair EcoRI/KpnI fragment comprising codons 1 to 62 of sub-unit IV of yeast cytochrome oxidase.

15. Process for inhibiting the production of pollen in selected higher plants, comprising the following steps: (a) inserting a hybrid nucleic acid sequence that is capable of modifying male fertility in plants having it incorporated therein, wherein said sequence comprises at least a coding region of an unedited mitochondrial gene from a higher plant, with which is associated a sequence capable of transferring the protein expressed by the said coding region to the mitochondrion, wherein: the coding region of the unedited mitochondrial gene is the wheat ATP6 gene in unedited form and ligated to a mitochondrial transporter sequence, wherein the hybrid nucleic acid sequence comprising the ATP 6 gene, when transformed into a recipient plant, causes male sterility; and wherein the nucleic acid sequence capable of transferring the said expressed protein to the mitochondrion is selected from the group consisting of: the fragments encoding yeast tryptophanyl tRNA synthetase, the .beta. sub-unit of *Nicotiana plumbaginifolia* ATPase, the maize ATP/ADP translocator, and a 303 base pair EcoRI/KpnI fragment comprising codons 1 to 62 of sub-unit IV of yeast cytochrome oxidase into the selected plants to form a transgenic plant of decreased male fertility; (b) regenerating and culturing the transgenic plants obtained in (a); and (c) measuring the production and the viability of pollen from said transgenic plants.

16. Process for restoring male fertility to transgenic male-sterile plants, comprising the following steps: (1) transforming a selected higher plant by introducing at least one copy of a hybrid nucleic sequence that is capable of modifying male fertility in plants having it incorporated therein, wherein said sequence comprises at least a coding region of an unedited mitochondrial gene from a higher plant, with which is associated a sequence capable of transferring the protein expressed by the said coding region to the mitochondrion, wherein: the coding region of the unedited mitochondrial gene is the wheat ATP6 gene in unedited form and ligated to a mitochondrial transporter sequence, wherein the hybrid nucleic acid sequence comprising the ATP 6 gene, when transformed into a recipient plant, causes male sterility; and wherein the nucleic sequence capable of transferring the said expressed protein to the mitochondrion is selected from the group consisting of: the fragments encoding yeast tryptophanyl tRNA synthetase, the .beta. sub-unit of *Nicotiana plumbaginifolia* ATPase, the maize ATP/ADP translocator, and a 303 base pair EcoRI/KpnI fragment comprising codons 1 to 62 of sub-unit IV of yeast cytochrome oxidase into a recipient plant, by means of a plasmid containing said sequence, whereby obtaining a transgenic male-sterile plant; (2) transforming the same higher plant as in (1), by introducing at least one copy of an antisense hybrid nucleic sequence comprising, in the reverse direction, at least the same coding region of the unedited plant mitochondrial gene as that contained in the said transgenic male-sterile plants obtained in (1), into a recipient plant, by means of a plasmid containing the said sequence, whereby obtaining transgenic male-fertile plants; and (3) crossing the transgenic male-sterile plants obtained in (1) and the male-fertile plants obtained in (2), in order to obtain hybrids.



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L14: Entry 1 of 16

File: USPT

Oct 31, 2000

DOCUMENT-IDENTIFIER: US 6140082 A

TITLE: Expression of gene products from genetically manipulated strains of bordetella

Brief Summary Text (7):

Particular biological properties of strains of Bordetella make them attractive hosts for the production of certain heterologous gene products. Thus, many of the antigens produced by B. pertussis are large, can be multimeric and may require post-translational assembly or processing. For example, the pertactin antigen is produced as a 93-kDa precursor and the mature protein is produced by excision of the N-terminal signal peptide and removal of a C-terminal fragment. Pertussis toxin is a 105 kDa exotoxin produced by B. pertussis, and is encoded by the TOX operon and consists of five polypeptide subunits (S1 to S5) arranged in the typical A--B structure of bacterial toxins. The S2, S3, S4 and S5 subunit form a pentamer (the B oligomer) which, when combined with the S1 subunit forms the holotoxin. For PT, for example, such complex assembly cannot be achieved in *E. coli* (ref. 22) and, for the 69 kd material, protein accumulated as insoluble inclusion bodies in *E. coli* (ref. 23). This intracellular expression in *E. coli* is to be contrasted with the secretion

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L2: Entry 25 of 32

File: USPT

Feb 2, 1999

DOCUMENT-IDENTIFIER: US 5866570 A

TITLE: Treatment of vascular leakage and related syndrome such as septic shock by administration of metalloproteinase inhibitors

Detailed Description Text (214):

This example evaluates the effects of immunotoxin administration on serum metalloproteinase levels. A Cynomolgous monkey, given the internal designation Monkey 4847 was injected intravenously with OLX-209, a Pseudomonas exotoxin based immunotoxin. The OLX-209 immunotoxin comprises a single chain antibody which specifically binds to erbB-2 fused via an oligopeptide linker to a fragment of Pseudomonas exotoxin lacking the binding domain, and further comprising a deletion of amino acids 365-380 of domain II, and a deletion of the last five amino acids of domain III, which are substituted by the tetrapeptide KDEL. After OLX-209 administration, the monkey was bled at 10, 30, 45, 60, 90, 120, 180 and 240 minutes after injection.

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L14: Entry 15 of 16

File: USPT

Aug 12, 1997

DOCUMENT-IDENTIFIER: US 5656488 A

TITLE: Recombinant avirulent salmonella antifertility vaccines

Detailed Description Text (191):

As above, the LT-B fusion vectors, pYA3048, which possesses a signal sequence so that the product is transported to the periplasm and (pYA3082, which lacks the signal sequence and will cause the product to remain in the cytoplasm, can be employed. The procedures for both vectors are the same. pYASP-10Nter, constructed as described above, is cut with NcoI followed by treatment with Klenow fragment to fill in the complement to the 5' overhang. The sequence is then cut with PstI in order to include the previously inserted termination stop codons in pYA3098stop. The pYA3048 and pYA3082 vectors are cleaved with ApaLI and digested by mung bean nuclease to result in blunt-ended molecules. The vectors are cut to completion with PstI. The insert and vector molecules are ligated together and introduced into .chi.6212 containing the lacI.sup.q gene on pYA232. The constructs are designated pYALT-B-SP-10NterPer and pYALT-B-SP-10NterCyt. The ability to synthesize a protein that reacts with antibodies to SP-10 and LT-B following IPTG induction is investigated, as well as the viability of cells grown continuously in the presence of IPTG. The construct with the fusion that permits stable, high-level expression with stability of the plasmid insert is used in subsequent studies. If the construct with the signal sequence is viable when grown in the presence of IPTG, cold osmotic shock and Western blot analysis are used to verify that the LT-B/SP-10 fusion is in the periplasmic space. It is then determined whether the fusion forms a pentamer in the periplasm. LT-B pentamers are stable up to 60.degree. C. in 0.1% SDS and do not react with anti-LT-B antibody following SDS polyacrylamide gel electrophoresis. The pentameric LT-B disassociates at 70.degree. C. or above in the presence of 0.1% SDS to yield monomeric molecules which now readily react with antisera against the LT-B monomer subunit. Thus, testing antigenicity following treatment at different temperatures can reveal whether pentamers do or do not form.

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L29: Entry 1 of 10

File: PGPB

Mar 20, 2003

DOCUMENT-IDENTIFIER: US 20030054012 A1

TITLE: PSEUDOMONAS EXOTOXIN A-LIKE CHIMERIC IMMUNOGENS FOR ELICITING A SECRETORY IGA-MEDIATED IMMUNE RESPONSE

## CLAIMS:

1. A method of eliciting a secretory IgA-mediated immune response in a subject comprising the step of administering to at least one mucosal surface of the subject a non-toxic Pseudomonas exotoxin A-like ("PE-like") chimeric immunogen comprising: (1) a cell recognition domain of between 10 and 1500 amino acids that binds to a cell surface receptor on the mucosal surface; (2) a translocation domain comprising an amino acid sequence substantially identical to a sequence of PE domain II sufficient to effect translocation to a cell cytosol; (3) a foreign epitope domain comprising an amino acid sequence of between 5 and 1500 amino acids that encodes a foreign epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum ("ER") retention domain that comprises an ER retention sequence.

11. The composition of claim 8 produced by administering to at least one mucosal surface of a subject a non-toxic Pseudomonas exotoxin A-like ("PE-like") chimeric immunogen comprising: (1) a cell recognition domain of between 10 and 1500 amino acids that binds to a cell surface receptor on the mucosal surface; (2) a translocation domain comprising an amino acid sequence substantially identical to a sequence of PE domain II sufficient to effect translocation to a cell cytosol; (3) a foreign epitope domain comprising an amino acid sequence of between 5 and 1500 amino acids that encodes a an epitope of HIV-1; and (4) an amino acid sequence encoding an endoplasmic reticulum ("ER") retention domain that comprises an ER retention sequence.

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Dec 24, 2002

CLAIMS:

1. A multidomain protein comprising, a target cell-specific binding domain, a translocation domain and a nucleic acid binding domain, wherein the translocation domain is derived from a diphtheria toxin but does not include the cytotoxic part of said diphtheria toxin, wherein the translocation domain is derived from amino acids 194-378 or 196-384 of said diphtheria toxin.
2. The multidomain protein according to claim 1, wherein said translocation domain is amino acids 194-378 or 196-384 of said diphtheria toxin.
3. The multidomain protein according to claim 1, further comprising an endoplasmic reticulum retention signal and a nuclear localization signal, wherein said protein has an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:35, SEQ ID NO:37, and SEQ ID NO:39.

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Dec 8, 1992

TITLE: Covalently-linked complexes and methods for enhanced cytotoxicity and imaging imaging

9. The covalently-linked complex of claim 1 wherein the enhancing moiety is a translocating/internalizing moiety, an anchoring peptide, an accessory moiety, an intracellular retention moiety, a combination peptide, a fusion peptide or a combination thereof.

10. The covalently-linked complex of claim 9 wherein the translocating/internalizing moiety is selected from the group consisting of aa1-aa2-aa2-aa3-EAALA(EALA).sub.4 -EALEALAA-amide, TAT protein 37-62 fragment, CFITKALGISYGRKKRRRQRRPPQGS, growth factor-derived peptides, peptides containing the sequence CMHIESLDSTYC or CMYIEALDKYAC, estrogens, anti-estrogens peptides of apolipoprotein A-1 and B, melittin, bombolittin, delta hemolysin, pardaxins, alamethicin, calcitonin, corticotrophin releasing factor, beta endorphin, glucagon, parathyroid hormone, pancreatic polypeptide, signal sequences, hidden hydrophobic domains, anti-clathrin antibody or fragments thereof, pore-forming proteins, and analogs, derivatives and combinations thereof.

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L14: Entry 9 of 16

File: USPT

Jan 26, 1999

DOCUMENT-IDENTIFIER: US 5863891 A

\*\* See image for Certificate of Correction \*\*

TITLE: Chimeric toxinsDetailed Description Text (2):

DAB.sub.486 -IL-2 is a chimeric toxin consisting of Met followed by amino acid residues 1 through 485 of mature DT fused to amino acid residues 2 through 133 of IL-2. The DT portion of the chimeric toxin DAB.sub.486 -IL-2 includes all of DT fragment A and the portion of DT fragment B extending to residue 485 of mature native DT. Thus DAB.sub.486 -IL-2 extends past the disulfide bridge linking Cys 461 with Cys 471. See FIG. 1a for the structure of DT. (The nomenclature adopted for IL-2-toxin is DAB.sub.486 -IL-2, where D indicates diphtheria toxin, A and B indicate wild type sequences for these fragments, and IL-2 indicates human interleukin-2 sequences. Mutant alleles are indicated by a number in parentheses following DAB. The numerical subscript indicates the number of DT-related amino acids in the fusion protein. Since the deletion of the tox signal sequence and expression from the trc promoter results in the addition of a methionine residue to the N-terminus, the numbering of DAB-IL-2 fusion toxins is +1 out of phase with that of native diphtheria toxin.)

*Breussis operon  
or Diphtheria*

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L14: Entry 10 of 16

File: USPT

Jul 28, 1998

DOCUMENT-IDENTIFIER: US 5786189 A

TITLE: Vaccine

Brief Summary Text (15):

Burnette et al., EP-A-306,318, published Mar. 8, 1989, report the subcloning and expression of individual B. pertussis toxin subunits in E. coli. Burnette et al. disclose that the S4 subunit could only be expressed upon removal of the signal peptide coding sequence. Burnette et al. also disclose S1 subunit analogs expressed in E. coli with modifications between amino acids Val.sup.7 to Pro.sup.14.



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L14: Entry 5 of 16

File: USPT

Oct 12, 1999

DOCUMENT-IDENTIFIER: US 5965406 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Recombinant DNAs encoding three-part hybrid proteins

Detailed Description Text (25):

The polypeptide encoded by the resulting NcoI-ApaI fragment lacks the natural cholera toxin signal sequence, having instead fmet-Gly followed by the mature A.sub.1 region of cholera toxin, followed by Gly-Ser-Gly-Pro. This construct can be cloned into a plasmid that encodes diphtheria toxin fragment B' fused to the human interleukin-2 gene (plasmid pPA123, FIG. 7). Plasmid pPA123 was constructed from plasmid pDW24 (Diane Williams, Ph.D. dissertation, Boston University School of Medicine, Department of Microbiology, Boston, Mass., 02118, 1989) as outlined in FIG. 7. Plasmid pDW24 encodes a diphtheria toxin fragment A-fragment B'-IL2 fusion protein that is expressed off the trc promoter in E. coli. The sequences encoding fragment A were deleted by digestion with the restriction endonucleases NcoI and NsiI. The following oligonucleotides were used to rebuild the fragment A/B disulfide loop (1.sub.1) sequence, introduce an ApaI site on the 5' end of the loop, and recreate the NcoI site encoding the translation-initiating ATG codon:

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L14: Entry 3 of 16

File: USPT

Feb 8, 2000

DOCUMENT-IDENTIFIER: US 6022950 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Hybrid molecules having translocation region and cell-binding region

Detailed Description Text (25):

The polypeptide encoded by the resulting NcoI-ApaI fragment lacks the natural cholera toxin signal sequence, having instead fmet-Gly followed by the mature A.sub.1 region of cholera toxin, followed by Gly-Ser-Gly-Pro. This construct can be cloned into a plasmid that encodes diphtheria toxin fragment B' fused to the human interleukin-2 gene (plasmid pPA123, FIG. 7). Plasmid pPA123 was constructed from plasmid pDW24 (Diane Williams, Ph.D. dissertation, Boston University School of Medicine, Department of Microbiology, Boston, Mass., 02118, 1989) as outlined in FIG. 7. Plasmid pDW24 encodes a diphtheria toxin fragment A-fragment B'-IL2 fusion protein that is expressed off the trc promoter in E.coli. The sequences encoding fragment A were deleted by digestion with the restriction endonucleases NcoI and NsiI. The following oligonucleotides were used to rebuild the fragment A/B disulfide loop (1.sub.1) sequence, introduce an ApaI site on the 5' end of the loop, and recreate the NcoI site encoding the translation-initiating ATG codon:

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L29: Entry 7 of 10

File: USPT

Jul 23, 2002

DOCUMENT-IDENTIFIER: US 6423513 B1

TITLE: Polynucleotides encoding protease-activatable pseudomonas exotoxin a-like proproteins

## CLAIMS:

1. A recombinant polynucleotide comprising a nucleotide sequence encoding a protease-activatable Pseudomonas exotoxin A-like ("PE-like") proprotein comprising:  
(a) a cell recognition domain of between 10 and 1500 amino acids that binds to an exterior surface of a targeted cell; (b) a modified PE translocation domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 280 to 344 of SEQ ID NO:2 and which effects translocation to a cell cytosol upon proteolytic cleavage, wherein the translocation domain comprises a cysteine-cysteine loop that comprises a protease activatable sequence cleavable by a protease and wherein the protease activatable sequence is refractory to cleavage by furin when incubated with furin at a 1:10 enzyme:substrate molar ratio at 25.degree. C. for 16 hours; (c) a cytotoxicity domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 400 to 613 of SEQ ID NO:2, the cytotoxicity domain having ADP-ribosylating activity; and (d) an endoplasmic reticulum ("ER") retention sequence.
2. The recombinant polynucleotide of claim 1, further comprising a nucleic acid sequence encoding a PE Ib-like domain comprising an amino acid sequence of between 5 and about 1500 amino acids, which amino acid sequence is positioned between the modified PE translocation domain and the cytotoxicity domain and which does not interfere with the ability of the PE-like proprotein to bind cells, translocate, or ribosylate ADP.
4. The recombinant polynucleotide of claim 2 wherein: (a) the cell recognition domain is an antibody coupled to the modified PE translocation domain through a peptide bond and wherein the antibody specifically binds a cancer cell surface marker; (b) the modified PE translocation domain has a PE domain II sequence (amino acids 253-364 of SEQ ID NO:2) modified with amino acid substitutions introducing the protease activatable sequence so as to cause cleavage by the protease between amino acids 279 and 280; and (c) the PE Ib-like domain, the cytotoxicity domain and the ER retention sequence together have the sequence of domains Ib and III of native native PE.

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L29: Entry 6 of 10

File: USPT

Jul 30, 2002

DOCUMENT-IDENTIFIER: US 6426075 B1

TITLE: Protease-activatable pseudomonas exotoxin A-like proproteins

## CLAIMS:

1. A protease-activatable Pseudomonas exotoxin A-like ("PE-like") proprotein comprising: (a) a cell recognition domain that binds to an exterior surface of a targeted cell; (b) a modified PE translocation domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 280 to 344 of SEQ ID NO:2 and which effects translocation to a cell cytosol upon proteolytic cleavage, wherein the translocation domain comprises a cysteine-cysteine loop that comprises a protease activatable sequence cleavable by a protease and wherein the protease activatable sequence is refractory to cleavage by furin when incubated with furin at a 1:10 enzyme:substrate molar ratio at 25.degree. C. for 16 hour; (c) a cytotoxicity domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 400 to 613 of SEQ ID NO:2, the cytotoxicity domain having ADP-ribosylating activity; and (d) an endoplasmic reticulum ("ER") retention sequence.
2. The PE-like proprotein of claim 1 wherein the modified PE translocation domain has a PE domain II sequence (amino acids 253-364 of SEQ ID NO:1) modified with amino acids substitutions introducing the protease activatable sequence so as to cause cleavage by the protease between amino acids 279 and 280.
8. The PE-like proprotein of claim 2 further comprising a PE Ib domain, and wherein said PE Ib domain, the cytotoxicity domain, and the ER retention sequence together have the sequence of domains Ib and III of native PE.
9. The PE-like proprotein of claim 3 wherein the cell recognition domain is coupled to the modified translocation domain through a peptide bond.
12. The PE-like proprotein of claim 8 wherein the cell recognition domain is an antibody coupled to the modified translocation domain through a peptide bond and wherein the antibody specifically binds a cancer cell surface marker.
13. A composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a protease-specific Pseudomonas exotoxin A-like ("PE-like") proprotein comprising: (a) a cell recognition domain that binds to an exterior surface of a targeted cell; (b) a modified PE translocation domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 280 to 344 of SEQ ID NO:2 and which effects translocation to a cell cytosol upon proteolytic cleavage, wherein the translocation domain comprises a cysteine-cysteine loop that comprises a protease activatable sequence cleavable by a protease and wherein the protease activatable sequence is substantially un-activatable by fibrin when incubated with furin at a 1:10 enzyme:substrate molar ratio at 25.degree. C. for 16 hours; (c) a cytotoxicity domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 400 to 613 of SEQ WD NO:2, the cytotoxicity domain having ADP-ribosylating activity; and (d) an endoplasmic reticulum ("ER") retention sequence.

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L23: Entry 5 of 12

File: USPT

Jul 30, 2002

DOCUMENT-IDENTIFIER: US 6426075 B1

TITLE: Protease-activatable pseudomonas exotoxin A-like proproteins

## CLAIMS:

1. A protease-activatable Pseudomonas exotoxin A-like ("PE-like") proprotein comprising: (a) a cell recognition domain that binds to an exterior surface of a targeted cell; (b) a modified PE translocation domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 280 to 344 of SEQ ID NO:2 and which effects translocation to a cell cytosol upon proteolytic cleavage, wherein the translocation domain comprises a cysteine-cysteine loop that comprises a protease activatable sequence cleavable by a protease and wherein the protease activatable sequence is refractory to cleavage by furin when incubated with furin at a 1:10 enzyme:substrate molar ratio at 25.degree. C. for 16 hour; (c) a cytotoxicity domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 400 to 613 of SEQ ID NO:2, the cytotoxicity domain having ADP-ribosylating activity; and (d) an endoplasmic reticulum ("ER") retention sequence.
13. A composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a protease-specific Pseudomonas exotoxin A-like ("PE-like") proprotein comprising: (a) a cell recognition domain that binds to an exterior surface of a targeted cell; (b) a modified PE translocation domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 280 to 344 of SEQ ID NO:2 and which effects translocation to a cell cytosol upon proteolytic cleavage, wherein the translocation domain comprises a cysteine-cysteine loop that comprises a protease activatable sequence cleavable by a protease and wherein the protease activatable sequence is substantially un-activatable by fibrin when incubated with furin at a 1:10 enzyme:substrate molar ratio at 25.degree. C. for 16 hours; (c) a cytotoxicity domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 400 to 613 of SEQ WD NO:2, the cytotoxicity domain having ADP-ribosylating activity; and (d) an endoplasmic reticulum ("ER") retention sequence.
16. A method for killing a cancer cell comprising contacting the cell with a protease-specific Pseudomonas exotoxin A-like ("PE-like") proprotein comprising: (a) a cell recognition domain that binds to an exterior surface of a targeted cell; (b) a modified PE translocation domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 280 to 344 of SEQ ID NO:2 and which effects translocation to a cell cytosol upon proteolytic cleavage, wherein the translocation domain comprises a cysteine-cysteine loop that comprises a protease activatable sequence cleavable by a protease and wherein the protease activatable sequence cysteine-cysteine loop is substantially un-activatable by furin when incubated with furin at a 1:10 enzyme:substrate molar ratio at 25.degree. C. for 16 hours; (c) a cytotoxicity domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 400 to 613 of SEQ ID NO:2, the cytotoxicity domain having ADP-ribosylating activity; and (d) an endoplasmic reticulum ("ER") retention sequence.

14. The composition of claim 13, further comprising a PE Ib-like domain, wherein:  
(a) the cell recognition domain is an antibody coupled to the modified PE translocation domain through a peptide bond and wherein the antibody specifically binds a cancer cell surface marker; (b) the modified PE translocation domain has a PE domain II sequence (amino acids 253-364 of SEQ ID NO:1) modified with amino acids substitutions introducing the protease activatable sequence so as to cause cleavage by the protease between amino acids 279 and 280; and (c) the PE Ib-like domain, the cytotoxicity domain and the ER retention sequence together have the sequence of domains Ib and III of native PE.
16. A method for killing a cancer cell comprising contacting the cell with a protease-specific Pseudomonas exotoxin A-like ("PE-like") proprotein comprising:  
(a) a cell recognition domain that binds to an exterior surface of a targeted cell;  
(b) a modified PE translocation domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 280 to 344 of SEQ ID NO:2 and which effects translocation to a cell cytosol upon proteolytic cleavage, wherein the translocation domain comprises a cysteine-cysteine loop that comprises a protease activatable sequence cleavable by a protease and wherein the protease activatable sequence cysteine-cysteine loop is substantially un-activatable by furin when incubated with furin at a 1:10 enzyme:substrate molar ratio at 25.degree. C. for 16 hours; (c) a cytotoxicity domain comprising an amino acid sequence with 80% or greater sequence identity to amino acids 400 to 613 of SEQ ID NO:2, the cytotoxicity domain having ADP-ribosylating activity; and (d) an endoplasmic reticulum ("ER") retention sequence.

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L23: Entry 9 of 12

File: USPT

Jan 26, 1999

DOCUMENT-IDENTIFIER: US 5863745 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Recombinant antibody-toxin fusion protein

## CLAIMS:

1. A method for achieving targeted cytotoxicity, comprising contacting cells targeted to be killed with a cytotoxic amount of an antibody-PE40 recombinant fusion protein, wherein said antibody is a single-chain Fv fragment (scFv) and said PE40 is a Pseudomonas exotoxin (PE) fragment omitting amino acids 1 through 252 and possessing at least the translocating and ADP ribosylating activity of PE, and wherein said cells targeted to be killed have receptors or antigens to which said antibody binds, a wherein said fusion protein has lower toxicity to ceus which lack receptors or antigens for the binding of said antibody.

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L14: Entry 1 of 16

File: USPT

Oct 31, 2000

US-PAT-NO: 6140082

DOCUMENT-IDENTIFIER: US 6140082 A

TITLE: Expression of gene products from genetically manipulated strains of bordetella

DATE-ISSUED: October 31, 2000

## INVENTOR-INFORMATION:

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Klein; Michel Henri	Willowdale			CA

## ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
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APPL-NO: 09/ 374597   [PALM]

DATE FILED: August 16, 1999

## PARENT-CASE:

REFERENCE TO RELATED APPLICATION This application is a continuation of application No. 08/393,334 filed Feb. 23, 1995 now abandoned.

INT-CL: [07] C12 P 21/06, C07 H 17/00, C07 K 14/00

US-CL-ISSUED: 435/69.1; 435/69.8, 435/320.1, 435/325, 435/252.3, 536/23.1, 530/350

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 435/69.8, 530/350, 536/23.1

FIELD-OF-SEARCH: 536/23.1, 435/69.1, 435/252.3, 435/320.1, 530/350

PRIOR-ART-DISCLOSED:

## U.S. PATENT DOCUMENTS

Search Selected

Search ALL

Clear

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
<input type="checkbox"/>	<u>5395764</u>	March 1995	Riboli et al.	
<input type="checkbox"/>	<u>5439810</u>	August 1995	Loosemore et al.	
<input type="checkbox"/>	<u>5942418</u>	August 1999	Loosmore et al.	425/69.1



## FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
336413	April 1989	EP	
368819	September 1989	EP	
453216	April 1991	EP	
523976	July 1992	EP	
2690459	October 1993	FR	
WO 95/28486	October 1995	WO	

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Bennetzen et al 1982. J. Biol Chem. 257:3026.  
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Kurosky et al 1997. J. Biol. Chem. 252:7257.

ART-UNIT: 163

PRIMARY-EXAMINER: Carlson; Karen Cochrane

ATTY-AGENT-FIRM: Sim &amp; McBurney

## ABSTRACT:

An expression system for expressing gene products from recombinant Bordetella strains and specific nucleic acid molecules useful in transforming Bordetella strains for such expression are described. A nucleic acid molecule may comprise a Bordetella promoter operatively coupled to a heterologous gene encoding a non-Bordetella gene product with the heterologous gene transcriptionally regulated by

the Bordetella promoter. The nucleic acid molecule may further comprise a further nucleic acid molecule encoding a leader sequence for secretion of the non-Bordetella Bordetella gene product. Another nucleic acid molecule may comprise a Bordetella promoter coupled to a nucleic acid sequence encoding a non-Bordetella leader sequence for secretion of a gene product, which may be a Bordetella gene product or a non-Bordetella gene product.

31 Claims, 15 Drawing figures

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L15: Entry 1 of 46

File: PGPB

Jun 27, 2002

PGPUB-DOCUMENT-NUMBER: 20020081713  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020081713 A1

TITLE: ADP-ribosylation factor-like proteins

PUBLICATION-DATE: June 27, 2002

## INVENTOR-INFORMATION:

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## ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE	CODE
Yung Shin Pharmaceutical Ind. Co., Ltd., Taiwan corporation					03

APPL-NO: 09/ 848813 [PALM]

DATE FILED: May 4, 2001

## RELATED-US-APPL-DATA:

Application 09/848813 is a continuation-of US application 09/217046, filed December 21, 1998, ABANDONED

INT-CL: [07] C12 N 1/18, C12 P 21/02

US-CL-PUBLISHED: 435/254.21; 435/69.1

US-CL-CURRENT: 435/254.21; 435/69.1

## ABSTRACT:

The invention relates to a transgenic knockout yeast which has a disruption in the gene encoding for a yeast ADP-ribosylation factor-like protein.

[0001] This application is a continuation, and claims the benefit of priority under 35 USC 120, of U.S. Application Ser. No. 09/217,046, filed Dec. 21, 1998. The disclosure of the prior application is considered part of, and is incorporated by reference in, the disclosure of this application.

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L14: Entry 2 of 16

File: USPT

Mar 21, 2000

DOCUMENT-IDENTIFIER: US 6040427 A

TITLE: Vaccine

Brief Summary Text (15):

Burnette et al., EP-A-306,318, published Mar. 8, 1989, report the subcloning and expression of individual B. pertussis toxin subunits in E. coli. Burnette et al. disclose that the S4 subunit could only be expressed upon removal of the signal peptide coding sequence. Burnette et al. also disclose S1 subunit analogs expressed in E. coli with modifications between amino acids Val.sup.7 to Pro.sup.14.